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1635



DOCKET NO.: ISIS-4847

PATENT

#9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED

In Re Application of:

Muthiah Manoharan

Confirmation No.: 3873

SEP 0 9 2002

Serial No.: 09/965,551

Group Art Unit: 1635

TECH CENTER 1600/2900

Filing Date: September 27, 2001

Examiner: Schultz, James

**For: CARBOHYDRATE OR 2'-MODIFIED OLIGONUCLEOTIDES HAVING
ALTERNATING INTERNUCLEOSIDE LINKAGES**

EXPRESS MAIL LABEL NO: EL568027053US

DATE OF DEPOSIT: September 3, 2002

EL568027053US

Box ☒ NON-FEE

☐ AF

Assistant Commissioner for Patents
Washington DC 20231

Sir:

REPLY TRANSMITTAL LETTER

Transmitted herewith for filing in the above-identified patent application is:

- ☐ A Preliminary Amendment.
- ☒ An Amendment Responsive to the Office Action Dated June 5, 2002.
- ☐ An Amendment Supplemental to the Paper filed _____.
- ☐ Other: _____.

- ☒ Applicant(s) has previously claimed small entity status under 37 CFR §1.27.
- ☐ Applicant(s) by its/their undersigned attorney, claims small entity status under 37 CFR §1.27 as:
- ☐ an Independent Inventor
 - ☐ a Small Business Concern
 - ☐ a Nonprofit Organization
- ☐ This application is no longer entitled to small entity status. It is requested that this be noted in the files of the U.S. Patent and Trademark Office.
- ☐ Loss of Entitlement Enclosed
- ☐ Substitute Pages _____ of the Specification are enclosed.
- ☐ An Abstract is enclosed.
- ☐ _____ Sheets of Proposed Corrected Drawings are enclosed.
- ☐ A Certified Copy of each of the following applications: _____
_____ is enclosed.
- ☒ An Associate Power of Attorney is enclosed.
- ☐ Information Disclosure Statement.
- ☐ Attached Form 1449.
 - ☐ A copy of each reference as listed on the attached Form PTO-1449 is enclosed herewith.
- ☐ Appended Material as follows: _____ .
- ☒ Other Material as follows: 1) Offensperger et al., EMBO J., 1993., 1993, 12, 1257-1262, "In vivo inhibition of duck hepatitis B virus replication and gene expression by

phosphorothioate modified antisense oligodeoxynucleotides"; 2) Simons et al., Nature, Nature, 1992, 359, 67-70, "Antisense c-myb oligonucleotides inhibit intimal arterial smooth muscle cell accumulation in vivo"; 3) Kitajima et al., Science, 1992, 258, 1792-1795, "Ablation of Transplanted HTLV-1 Tax-Transformed Tumors in Mice by Antisense Inhibition of NF-KB"; 4) Monia et al., Nature Med., 1996, 2, 668, "Antitumor activity of a phosphorothioate antisense oligodeoxynucleotide targeted against C-raf kinase"; 5) Oberbauer et al., Proc. Natl. Acad. Sci. USA, 1996, 93, 4903, "In vivo suppression of the renal Na⁺/P_i cotransporter by antisense oligonucleotides ; 6) Monia et al., Proc. Natl. Acad. Sci. USA, 1996, 93, 15481, "Sequence-specific antitumor activity of a phosphorothioate oligodeoxyribonucleotide targeted to human C-raf kinase supports an antisense mechanism of action in vivo"; 7) Cucco et al., Cancer Res., 1996, 56, 4332, "In Vitro and in Vivo Reversal of Multidrug Resistance in a Human Leukemia-resistant Cell Line by mdrl Antisense Oligodeoxynucleotides"; 8) Offensperger et al., Antisense Therapy of Hepatitis B Virus Infection, 1996, Agrawal Ed., Humana Press Inc. Tolowa, NJ, pp. 143-158, "Antisense Therapy of Hepatitis B Virus Infection - In Vivo Analyses in the Duck Hepatitis B Virus Model"; 9) Sun et al., Br. J. Pharmacol., 1996, 118, 131, "Effects of phosphorothioated neuropeptide Y Y₁-receptor antisense oligodeoxynucleotide in conscious rats and in human vessels"; 10) Neurath et al., Nature Med., 1996, 2, 998-1004, "Local administration of antisense phosphorothioate oligonucleotides to the p65 subunit of NF-kB abrogates established experimental colitis in mice"; 11) Leonetti et al., J.N.C.I., 1996, 88, 419, "Antitumor Effect of c-myc Antisense Phosphorothioate Oligodeoxynucleotides on Human Melanoma Cells In Vitro and in Mice; and 12) Del Bufalo et al., Br. J. Cancer, 1996, 74, 387, "Effect of cisplatin and c-myb antisense phosphorothioate oligodeoxynucleotides combination on a human colon carcinoma cell line in vitro and in vivo".

FEE CALCULATION

☒ No Additional Fee is Due.

				SMALL ENTITY		NOT SMALL ENTITY	
	REMAINING AFTER AMENDMENT	HIGHEST PAID FOR	EXTRA	RATE	FEE	RATE	FEE
TOTAL CLAIMS	21	21 (20 MINIMUM)	0	\$9 EACH	\$ 0	\$18 EACH	\$
INDEP. CLAIMS	3	3 (3 MINIMUM)	0	\$42 EACH	\$ 0	\$84 EACH	\$
FIRST PRESENTATION OF MULTIPLE DEPENDENT				\$140	\$ 0	\$280	\$
<input type="checkbox"/> ONE MONTH EXTENSION OF TIME				\$55	\$ 0	\$110	\$
<input type="checkbox"/> TWO MONTH EXTENSION OF TIME				\$200	\$ 0	\$400	\$
<input type="checkbox"/> THREE MONTH EXTENSION OF TIME				\$460	\$ 0	\$920	\$
<input type="checkbox"/> FOUR MONTH EXTENSION OF TIME				\$720	\$ 0	\$1440	\$
<input type="checkbox"/> FIVE MONTH EXTENSION OF TIME				\$980	\$ 0	\$1960	\$
<input type="checkbox"/> LESS ANY EXTENSION FEE ALREADY PAID				minus	(\$ 0)	minus	(\$)
<input type="checkbox"/> TERMINAL DISCLAIMER				\$55	\$ 0	\$110	\$
<input type="checkbox"/> OTHER FEE OR SURCHARGE AS FOLLOWS:					0		
TOTAL FEE DUE					0		\$

- ☐ A check is enclosed in the foregoing amount due.
- ☐ Petition is hereby made under 37 C.F.R. 1.136(a) (fees: 37 C.F.R. § 1.17(a)(1)-(4) to extend the time for response to the Office Action of @@ to and through @@ comprising an extension of the shortened statutory period of @@ month(s).
- ☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is

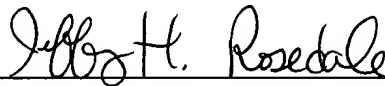
further authorized to charge any fees related to any such extension of time to Deposit Account 23-3050. This sheet is provided in duplicate.

- ☒ The Commissioner is authorized to charge payment of the following fees and to refund any overpayment associated with this communication or during the pendency of this application to Deposit Account 23-3050. This sheet is provided in duplicate.
- ☐ The foregoing amount due for filing this paper.
- ☒ Any additional filing fees required, including fees for the presentation of extra claims under 37 C.F.R. 1.16.
- ☒ Any additional patent application processing fees under 37 C.F.R. 1.17 or 1.20(d).

SHOULD ANY DEFICIENCIES APPEAR with respect to this application, including deficiencies in payment of fees, missing parts of the application or otherwise, the U.S. Patent and Trademark Office is respectfully requested to promptly notify the undersigned.

Date:

September 3, 2002



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